REMARKS

Claims 1-38 were pending in the application. Claims 30-34 have been cancelled. Claims 39-48 have been added. Claims 1-3, 6, 9, 11, 21-24, 28, 35 and 38 have been amended to clarify the invention. Support for the amendment of claims 1, 21-24, 35 and 38 and new claims 39-48 may be found throughout the specification and claims as originally filed. No new matter has been added.

Accordingly, upon entry of the present amendment, claims 1-29, 35, and 37-48 will be pending. Cancellation of and/or amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's objections and/or rejections. The cancellation of and/or amendments to the claims are being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application.

Submission of Priority Document

Applicants submit herewith a copy of the priority document GB 0107901.1, filed on March 29, 2001.

Rejection of Claims 30-38 under 35 U.S.C. § 112, first paragraph

Claims 30-38 have been rejected on the ground that the specification, "while being enabling for treating lung cancer, does not reasonably provide enablement for treatment of all types of diseases of the instant claims." Claims 30-34 have been cancelled, thus rendering their rejection moot.

Claims 35-38 are directed to methods of treating CDK dependent proliferative disorders by administering a compound of formula I. These claims are fully enabled by the instant specification. For Example, Applicants teach methods for determining the ability of the compounds of the invention to inhibit a panel of protein kinases (*e.g.*, Example 17). Furthermore, Table 1 gives CDK2/cyclin E IC_{50} values for 35 compounds of the invention. In addition, the specification describes an assay which shows the anti-proliferative effects of selected compounds of the invention (*e.g.*, Example 18). Data from this assay are presented for over 20 compounds of the invention in Table 2. Therefore, the specification provides sufficient information to allow the skilled artisan to identify compounds of the invention which are capable of inhibiting a CDK kinase which have an antiproliferative effect. The skilled artisan would be able to appreciate that compounds useful in inhibiting a CDK kinase and which have an antiproliferative effect

would be useful agents for treating CDK dependent proliferative disorders, as claimed by Applicants.

In addition, Applicants' claims are directed to methods of treating a subject for a CDK dependent proliferative disorder by administering a compound of the invention, such that the CDK dependent proliferative disorder is treated. Therefore, Applicants' claimed invention is directed ***only*** to methods wherein treatment of a CDK dependent proliferative disorder actually occurs after administration of the compound of the invention, and ***not*** to methods wherein treatment does not occur. Therefore, Applicants submit that the scope of the currently pending claims is fully enabled by the specification and respectfully request that this rejection of claims 35-38 be withdrawn.

Rejection of Claims 1-38 under 35 U.S.C. § 112, second paragraph

Claims 1-38 have been rejected under 35 U.S.C. § 112, second paragraph, "as being indefinite for failing to particularly and distinctly claim the subject matter which Applicant[s] regard as the invention."

In particular, the Examiner found the second proviso statement in claim 1 "not to be clear" and "it appears that there is some phrase missing before "4-ethyl, 3-methyl..." Applicants respectfully submit that this rejection no longer pertains to the claim as currently amended.

In addition, the Examiner found that the recitation of "a compound...**and** the pharmaceutically acceptable salts thereof" to be unclear. Applicants respectfully submit that this rejection of claim 1 no longer pertains to the claim as currently amended.

The Examiner also found the word "preferably" to be unclear in claims 21 and 22. It is respectfully submitted that claims 21 and 22 no longer recite the word "preferably."

The Examiner also rejected claims 30-34 as being indefinite for "merely recit[ing] a use without any active, positive steps delimiting how this use is actually practiced." It is respectfully submitted that claims 30-34 have been cancelled thus rendering their rejection moot.

Therefore, Applicants respectfully request that this rejection of claims 1-38 under 35 U.S.C. § 112, second paragraph, be withdrawn.

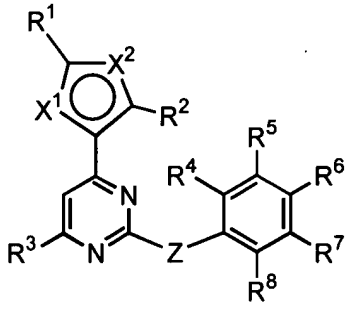
Rejection of Claims 30-34 under 35 U.S.C. § 101

Claims 30-34 were rejected under 35 U.S.C. § 101 because "the claimed recitation of a use...results in an improper definition of a process." Claims 30-34 have been cancelled, thus rendering their rejection moot.

Rejection of Claims 1, 3-5, 9-11, and 28-35 under 35 U.S.C. §102(b)

Claims 1, 3-5, 9-11, and 28-35 were rejected under 35 U.S.C. § 102(b), as being anticipated by Torley *et al.* EP 233 461. Claims 30-34 have been cancelled, thus rendering their rejection moot.

Claim 1 and its dependent claims are directed to compounds of the general formula I:



I

wherein:

X^1 is CR^9;

X^2 is NR^{10};

Z is NH;

R^1, R^2, R^3 R^9 and R^{10} are independently H, alkyl, aryl, aralkyl, heterocycle, halogeno, NO_2, CN, OH, alkoxy, aryloxy, (R''')nNH$_2$, (R''')nNH-R', (R''')nN-(R')(R''), NH-aryl, N-(aryl)$_2$, COOH, COO-R', COO-aryl, CONH$_2$, CONH-R', CON-(R')(R''), CONH-aryl, CON-(aryl)$_2$, SO_3H, SO_2NH_2, CF_3, CO-R', or CO-aryl, wherein alkyl, aryl, aralkyl and heterocycle groups may be further substituted with one or more groups selected from halogeno, NO_2, CN, OH, O-methyl, NH_2, COOH, CONH$_2$ and CF_3;

R^4, R^5, R^7, and R^8 are independently from each other H, substituted or unsubstituted lower alkyl, halogeno, NO_2, CN, OH, substituted or unsubstituted alkoxy, NH_2, NH-R', N-(R')(R''), COOH, COO-R', CONH$_2$, CONH-R', CON-(R')(R''), SO_3H, SO_2NH_2, or CF_3;

R^6 is H, substituted or unsubstituted lower alkyl, halogeno, NO_2, CN, OH, substituted or unsubstituted alkoxy, NH_2, NH-R', N-(R')(R''), COOH, COO-R', SO_3H, SO_2NH_2, or CF_3;

wherein R' R'' and R''' are each independently alkyl groups that may be the same or different and n is 0 or 1; or a pharmaceutically acceptable salt thereof. Claim 29 is directed to pharmaceutical compositions comprising a compound of claim 1.

Claim 35 is directed to a method for treating a CDK dependent proliferative disorder using compounds of claim 1.

Torley *et al.* describes the use of 4-(pyrrol-2-yl), 5, 6-substituted-2-pyrimidinamines for the treatment of pulmonary, inflammatory, allergic, diabetes and cardiovascular disorders.

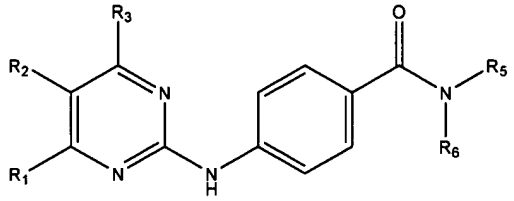
Applicants respectfully submit that Torley *et al.* fails to teach or suggest the compounds of claim 1, as currently amended, methods of using the claimed compounds, nor pharmaceutical compositions comprising the claimed compounds. Applicants claim compounds wherein the pyrimidine is substituted by a pyrrol-3-yl group (e.g., compounds wherein X^1 is CR^9 and X^2 is NR^{10}), while in contrast Torley *et al.* only describes pyrimidine compounds substituted with a 2-pyrrolyl group.

Therefore, Applicants respectfully request that this rejection of the claims 1, 3-5, 28, 29, and 35 under 35 U.S.C. § 102(b) be withdrawn.

Rejection of Claims 1, 3-4, and 29-35 under 35 U.S.C. § 102(e)

Claims 1, 3-4, and 29-35 were rejected under 35 U.S.C. §102(e) as being anticipated by Kois *et al.* (U.S. Patent Appln. No. 2003/0203926). Claims 1, 3-4, and 29-35 have been described above. Claims 30-34 have been cancelled, thus rendering their rejection moot.

Kois *et al.* is directed to the use of anilinopyridimidine derivatives as IKK inhibitors. The compounds described in Kois *et al.* are of the formula:



wherein R_1 may be heteroaryl, including pyrrolyl.

Applicants respectfully submit that Kois *et al.* fails to teach or suggest the compounds of claim 1, as currently amended, methods of using the compounds to treat CDK dependent proliferative disorders, and pharmaceutical compositions comprising them. Applicants claim compounds wherein the phenyl group is substituted at the 4-position by H, substituted or unsubstituted lower alkyl, halogeno, NO_2, CN, OH, substituted or unsubstituted alkoxy, NH_2, NH-R', N-(R')(R''), COOH, COO-R', SO_3H, SO_2NH_2, or CF_3, while in contrast Kois *et al.* only describes compounds substituted with $CONR_6R_5$.

Therefore, Applicants respectfully request that this rejection of claims 1, 3, 4, and 29, and 35 under 35 U.S.C. § 102(e) be withdrawn.

Rejection of Claim 1, 3-5, 9-11, and 28-35 under 35 U.S.C. § 103(a)

Claims 1, 3-5, 9-11, and 28-35 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Torley *et al.* According to the Examiner, the claims "include compounds that differ by a -CH_2 group." Claims 1, 3-5, 9-11, 28, 29, and 35 and the disclosure in Torley *et al.* have been described above. Claims 30-34 have been cancelled, thus rendering their rejection moot.

Applicants submit that the claims as currently pending differ from the compounds described in Torley *et al.* by more than "a -CH_2 group." Applicants submit that the present invention would not have been obvious to an ordinarily skilled artisan in view of Torley *et al.*, because Torley *et al.* fails to teach or suggest the compounds wherein the pyrimidine is substituted by a pyrrol-3-yl group (e.g., compounds wherein X^1 is CR^9 and X^2 is NR^{10}). Furthermore, it would not have been obvious to an ordinarily skilled artisan in view of Torley *et al.* to treat CDK dependent proliferative disorders using the instant compounds, because Torley *et al.* neither teaches nor suggests the use of any compounds for the treatment of CDK dependent proliferative disorders.

Rejection of Claims 1-2, and 29-38 under 35 U.S.C. § 103(a)

Claims 1-2, and 29-38 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Cao *et al.* (U.S. Patent Application No. 2003/0092714). Claims 1, 2, 29, and 35-38 have been described above. Claims 30-34 have been cancelled, thus rendering their rejection moot.

According to the Examiner, "the reference teaches compounds of pyrimidyl compounds, see formula III' in page 10 wherein the Sp is a pyrrole and further the compound 1 (page 17) and compound 119 (page 27) in Table 1A...Since the instantly claimed compounds differ only by the positions of the substituents, they are positional isomers of the reference compounds. It would have been obvious to one having ordinary skill in the art at the time of the invention to prepare the instantly claimed compounds because they are isomers of the reference compounds."

Applicants submit that it is only through the improper use of hindsight that the instant compounds would be obvious in view of Cao *et al.* Cao *et al.* describes over 200 compounds in their application and provides no biological data for compounds 1 or 119. Cao *et al.* teaches away from the present invention by showing that compounds with substantially different structures have the best biological activity in the described assays. It would not have been obvious to an ordinarily skilled artisan to select the compounds

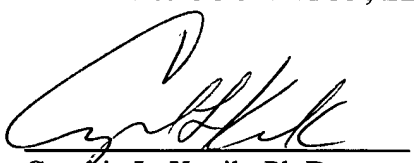
cited by the Examiner and then synthesize positional isomers to arrive at the claimed compounds or methods of using the claimed compounds.

Therefore, Applicants respectfully request that this rejection of claims 1, 2 and 29, and 35-38 under 35 U.S.C. § 103(a) be withdrawn.

SUMMARY

In view of the remarks set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicant's Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Respectfully submitted,
LAHIVE & COCKFIELD, LLP



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